NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE
Health Technology Appraisal

Abemaciclib for adjuvant treatment of hormone receptor-positive, HER2-negative, node-positive early breast cancer ID3857

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of abemaciclib within its marketing authorisation for adjuvant treatment of hormone receptor-positive, HER2-negative, node-positive early breast cancer.

Background

Breast cancer arises from the tissues of the ducts or lobules of the breast. Breast cancer is described as 'early' if it is restricted to the breast, or the breast and nearby lymph nodes, and has not spread to other parts of the body.

In 2017, there were approximately 46,109 new diagnoses of breast cancer in England.[1] In 2017 in England, there were 10,219 deaths from breast cancer.[2] There were approximately 36,508 cases of early breast cancer in the UK in 2017 according to the National Cancer Registration and Analysis Service.[3] Most (80%) breast cancers are hormone receptor-positive and around two-thirds are oestrogen receptor positive.[4] Between 80-85% of women with breast cancer will have HER2-negative tumours.[5]

Treatment may depend on whether the cancer cells have particular receptors (hormone receptor status or HER2 status), the extent of the disease, and previous treatments.

Adjuvant therapy is used to reduce the risk of the cancer coming back after surgery. The decision about whether to have adjuvant therapy is based on the assessment of the risk of the cancer coming back and the potential benefits and side effects of the treatment. NICE guideline 101 recommends adjuvant endocrine therapy (tamoxifen or aromatase inhibitors such as anastrozole and letrozole) for hormone receptor-positive early breast cancer.. It also recommends considering ovarian function suppression for premenopausal women and extended endocrine therapy (total duration of endocrine therapy of more than 5 years). Adjuvant chemotherapy (a regimen containing both a taxane and an anthracycline), adjuvant radiotherapy and adjuvant bisphosphonate therapy (for post-menopausal women) are also recommended for early breast cancer.

The technology

Abemaciclib (Verzenio, Lilly) is an inhibitor of cyclin-dependent kinases 4 and 6, which prevents DNA synthesis by prohibiting progression of the cell cycle from G1 to S phase. It is administered orally.

Abemaciclib does not currently have marketing authorisation in the UK for adjuvant treatment of hormone receptor-positive, HER2-negative, node positive early breast cancer. It has been studied in clinical trial in combination with standard adjuvant endocrine therapy compared to standard adjuvant endocrine therapy alone, in adults

with hormone receptor-positive, HER2-negative, node positive early breast cancer that are at high risk of recurrence after definitive surgery of the primary breast tumour.

Abemaciclib has a marketing authorisation in the UK for the treatment of women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2) locally advanced or metastatic breast cancer:

- in combinations with an aromatase inhibitor;
- or in combination with fulvestrant as initial endocrine-based therapy;
- or in combination with fulvestrant in women who have received prior endocrine therapy.

In pre- or perimenopausal women, the endocrine therapy should be combined with a luteinising hormone-releasing hormone (LHRH) agonist.

Intervention(s)	Abemaciclib in combination with standard endocrine therapy
Population(s)	Adults with hormone receptor-positive, HER2-negative, node-positive early breast cancer after definitive surgery of the primary breast tumour at high risk of recurrence.
Comparators	Standard endocrine therapy
Outcomes	The outcome measures to be considered include: • overall survival • invasive disease-free survival • recurrence-free survival • response rate • adverse effects of treatment • health-related quality of life.

Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	The availability and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	Related Technology Appraisals: None. Related Guidelines: Early and locally advanced breast cancer: diagnosis and management (2018) NICE guideline 101 Suspected cancer: recognition and referral (2015, updated 2020) NICE guideline 12 Familial breast cancer: classification, care and managing breast cancer and related risks in people with a family history of breast cancer (2013, updated 2019) NICE guideline CG164 Related Interventional Procedures: Endoscopic mastectomy and endoscopic wide local excision for breast cancer (2009) NICE interventional procedures guidance 296 Image-guided radiofrequency excision biopsy of breast lesions (2009) NICE interventional procedures guidance 308 Endoscopic axillary lymph node retrieval for breast cancer (2005) NICE interventional procedures guidance 147 Interstitial laser therapy for breast cancer (2004) NICE

	interventional procedures guidance 89 Related Public Health Guidance/Guidelines: MammaTyper in vitro diagnostic test for determining breast cancer subtypes (2018) NICE MedTech Innovation briefing 135 Early breast cancer (preventing recurrence and improving survival): adjuvant bisphosphonates (2017) NICE evidence summary 15 Axxent electronic brachytherapy system for early stage breast cancer (2016) NICE MedTech innovation briefing 76 Related Quality Standards: Suspected cancer (2016) NICE quality standard 124 Breast cancer (2011) NICE quality standard 12 Related NICE Pathways: Early and locally advanced breast cancer (2020) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2018) NHS England Funding and Resource 2018/19: Supporting 'Next Steps for the NHS Five Year Forward View' NHS England (2016) Radiotherapy after primary cancer for breast cancer. Clinical Commissioning Policy. Reference: 16038/P NHS England (2018) Manual for prescribed specialised services 2018/19 Chapter 31: Breast radiotherapy injury rehabilitation service (a discrete cohort of adult females), pp103-4 Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1

Questions for consultation

Have all relevant comparators for abemaciclib been included in the scope?

Which treatments are considered to be established clinical practice in the NHS for the adjuvant treatment of hormone receptor-positive, HER2-negative, node-positive early breast cancer?

Are the outcomes listed appropriate?

Are there any subgroups of people in whom abemaciclib is expected to be more clinically effective and cost effective or other groups that should be examined separately?

What is the definition of high risk early breast cancer? Is the definition used in the trial used routinely in UK clinical practice?

Trial definition of high risk:

- Pathologic lymph node involvement and at least one of the following indicating a higher risk of recurrence:
    - 4 or more positive axillary lymph nodes
    - Tumor size of at least 5 centimetres
    - Grade 3 defined as at least 8 points on the Bloom Richardson grading system
    - Ki-67 index by central analysis of ≥20% on untreated breast tissue

Where do you consider abemaciclib will fit into the existing, Early and locally advanced breast cancer (2020) NICE pathway?

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which abemaciclib will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider abemaciclib to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of abemaciclib can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. Office for National Statistics (2019) Cancer registration statistics, England, 2017. Accessed January 2021.

2. Office for National Statistics. Death Registrations Summary Statistics, England and Wales, 2017. Accessed January 2021.

3. National Cancer Registration and Analysis Service (NCRAS). Stage breakdown by CCG 2017. London: Public Health England, 2017. Accessed January 2021.

4. Dewis R and Gribbin J (2009) Breast cancer: diagnosis and treatment, an assessment of need. Cardiff: National Collaborating Centre for Cancer. Accessed January 2021.

5. Macmillan Cancer Support Receptors for HER2 Accessed January 2021.